UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,688	01/07/2002	Yong Hua Zhu	LOMAU.143A	5449

20995 7590 06/04/2003

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	10

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/041,688	Applicant(s) ZHU ET AL.	
	Examiner Isis Ghali	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6,7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The receipt is acknowledged of applicants' preliminary amendment A and IDS, both filed 07/08/2002; declaration fee and request for extension of time, both filed 07/15/2002; formal drawing and preliminary amendment B, both filed 10/01/2002; and IDS, filed 01/14/2003.

Specification

1. The use of the trademarks "Dermabond™", "Vetbond™", "Crazy Glue™", "Pluronic™", "Triton™", and "Rapamune®", have been noted in this application. It should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Drawings

2. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the

color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Claim Objections

3. Claims 2, 3, 14 and 15 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 1 and 12 recite "cyanoacylate" that is an acrylate containing "cyano" group, while the dependent claims 2 and 3 that depend on claim 1; and claims 14 and 15 that depend on claim 12, they all recite butyl and octyl acrylate in general and not cyanoacrylate in particular. Thus, the dependent claims not only failed to further limit the independent claims from which they depend, but also they broadened the scope of the independent claims 1 and 12. The examiner suggests amending the dependent claims 2, 3, 14 and 15 to recite the cyanoacrylate to be consistent with applicants' disclosure.

For examination purpose, the claims 2, 3, 14, and 15 are interpreted to recite cyanoacrylate.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2, 3, 14, and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using butyl and octyl cyanoacrylate adhesive in the composition of the present invention, does not reasonably provide enablement for the use of butyl and octyl acrylate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the breadth of the claims; the state of the prior art; the relative skill of those in the art; the amount of direction or guidance presented; the predictability or unpredictability of the art; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The nature of the invention: The nature of the invention is the use of cyanoacrylate adhesive including butyl and octyl cyanoacrylate for sealing wound. The entire specification disclosed cyanoacrylate adhesive that is an acrylate containing "cyano" group. In page 19, last paragraph and page 20 first paragraph of the present application, applicants disclosed butyl cyanoacrylate and octyl cyanoacrylate. Nowhere in the specification applicants disclosed butyl acrylate or octyl acrylate.

The breadth of the claims: The claims are very broad. The claims encompass a wide class of the acrylates. Acrylate includes cyanoacrylate, methacrylate, alkyl acrylate, polyacrylate, etc.

The state of the prior art: The state of the art does not recognize the butyl and octyl acrylate as adhesives for wound sealing, but recognized butyl and octyl cyanoacrylate, see US 5,811,091, col.5, lines 26-38; col.9, lines 1-14. The art also recognized butyl and octyl acrylate as tackyfing agent as disclosed by US 6,198,016, in col.7, lines 24-35, where the reference teaches butyl and octyl acrylates used to add tack to the adhesive composition.

The relative skill of those in the art: The relative skill of those in the art is high.

The amount of direction or guidance presented: The specification provides no guidance, in the way written description, on the butyl or octyl acrylate used in the composition used as wound sealant of present invention. It is not obvious from the disclosure of cyanoacylate if the acrylates will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must

appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

The predictability or unpredictability of the art: The lack of guidance from the specification and from the prior art with regard to sealing the wound with butyl and octyl acrylate makes practicing the claimed invention unpredictable in the terms of using butyl and octyl acrylate.

The presence or absence of working examples: The specification discloses only butyl and octyl cyanoacrylate, pages 19 and 20. No working examples to show using butyl and octyl acrylate. Therefore, the specification has enabled butyl and octyl acrylate claimed in claims 2, 3, 14, and 15.

The quantity of experimentation necessary: The art demonstrates cyanoacrylates for wound sealing and not acrylates. Therefor, the practitioner would turn to trial and error experimentation to practice the instant composition for sealing a wound without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

For examination purposes, claims 2 and 14 are interpreted as butyl cyanoacrylate, and claims 3 and 15 are interpreted as octyl cyanoacrylate.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 2, 3, and 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 3, 14 and 15 are confusing as they recite butyl and octyl acrylate that are not adhesive as an adhesive wound sealant, while applicants disclosed butyl and octyl cyanoacrylate in the specification. Clarification is requested.

For examination purposes, claims 2 and 14 are interpreted as butyl cyanoacrylate, and claims 3 and 15 are interpreted as octyl cyanoacrylate.

Claim 12 recites the step of "approximating the wound"; and it is not clear to the examiner what applicants meant by this phrase because the word "approximating" means approaching, coming near or estimating. Thus, the claim can read as coming closer to the wound or estimating the wound as far as the site whether external or internal, depth or size, etc. The claim also recites applying the adhesive composition to the tissue surrounding the wound and curing it, whereby the wound is sealed. This recitation is confusing as how the wound gets sealed if the adhesive is applied to the tissue surrounding the wound and not to the wound itself. Clarification is requested.

For examination purposes claim 12 is interpreted as the method of sealing a wound comprises approaching the wound and applying composition comprising cyanoacrylate, substance, and defect forming agent to the wound, and curing the adhesive.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 4, 5, 7-9, 12, 16, 17, 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/10374 ('374).

The above claims read as composition comprising cyanoacrylate, pore forming agent and antibiotic (claim 1, 4, 5, 7-9); and method for sealing wound comprising the steps of approaching the wound, applying the above composition and curing the composition (claims 12, 16, 17, 19-21).

WO '374 disclosed in situ polymerizing (*in situ* curing) biomedical implant material and a method for repair of mammalian tissue using the same biomedical material (abstract; page 8, line 35; page 9, line 1). The material comprises cyanoacrylate adhesive, hydrophilic porosifying agent and antibiotic (page 6, lines 9, 16-17; page 7, line 1; page 8, line 23 till page 9, line 2). The hydrophilic porosifying agent includes polyethylene glycol that dissolve *in situ* as a result of exposure to an aqueous

environment, e.g. body fluids are aqueous (page 4, lines 20-23). The *in situ* polymerizing implant material is introduced into the repair site (reads on wound) by variety of means and is used as a sealant in anatomic regions where it would be difficult to use a pre-cast dressing (page 12, lines 12-19). Introducing the *in situ* polymerizing implant material into the repair site reads on the step of "approximating the wound" in claim 12. Polymerization *in situ* reads on the step of curing the adhesive in claim 12.

Thus, the limitation of claims 1, 4, 5, 7-9, 12, 16, 17, 19-21 are met by WO '374.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO '374.

The teachings of the reference are discussed above. Although the reference teaches that the porosifying agent dissolves in the aqueous environment, i.e. the body fluid, but the reference does not teach the delivery of the substance to the tissue.

However, it is implied in the teaching of the reference in the teaching of the pre-cast system in the form of occlusive dressing or burn dressing that they deliver active agents such as anti-microbials (page 12, lines 22-30). It is expected from the implanted composition that polymerize *in situ* and comprises hydrophilic pore forming agent and substance to deliver the substance through the pores after the pore-forming agent dissolves.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a method for sealing wound comprising approaching the wound and applying composition comprising cyanoacrylate, pore forming agent and substance where the substance is delivered via the pores formed by removal of the pore forming agent, because the reference teaches that the substance to be delivered can be antibiotics that control sepsis of the wound, as desired by applicants, with reasonable expectation of the method not only to seal the wound, but also prevent its sepsis with the subsequent drawbacks.

13. Claims 2, 3, 14, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO '374 in view of US 5,811,091 ('091).

The teachings of WO '374 are discussed above.

WO '374 does not teach the cyanoacrylate as butyl or octyl cyanoacrylate as in claims 2, 3, 14, and 15.

US '091 teaches a composition comprising cyanoacrylates with the most preferred compounds include butyl and octyl cyanoacrylate because they bond the human skin tissue without causing histotoxicity or cytotoxicity (col.5, lines 26-49). The composition is useful for topically covering non-suturable wounds (col.8, line 4).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver the composition for wound sealing comprising cyanoacrylate, pore forming agent and active substance as disclosed by WO '374, and select butyl and octyl cyanoacrylate as taught by US '091, motivated by the teaching of US '091 that the butyl and octyl cyanoacrylate bond the human skin tissue without causing histotoxicity or cytotoxicity, with reasonable expectation of having a safe compatible wound sealing composition that successfully seals non-suturable wounds.

14. Claims 2, 3, 10, 11,14, 15, and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO '374 in view of WO 96/00760 ('760).

The teachings of WO '374 are discussed above.

WO '374 does not teach the cyanoacrylate as butyl or octyl cyanoacrylate as in claims 2, 3, 14, and 15; the anti-degradation agents claimed in claims 10, 11, 23 and 24; or the wound as a lacerated wound as in claim 22.

WO '760 teaches a biocompatible composition comprising pH modifier and cyanoacrylate monomer useful as biomedical and surgical adhesive and sealant (abstract; page 5, line 17). The advantageous monomers of the composition are butyl and octyl cyanoacrylate, as claimed in claims 2, 3, 14, 15, as they form a composition of adequate flexibility and strength to withstand normal movement of the tissue and a bond strength that is maintained as natural tissue healing proceeds (page 6, lines 15-19; page 18, lines 23-32). The pH modifier regulates the polymer biodegradation by regulating the pH of the in vivo environment of the biocompatible composition and makes it proceeds more slowly than it does at a physiological pH, this reads on anti-degradation agents claimed in claims 10 and 23, resulting in retarding the rate of release of the degradation products, thereby reducing their toxic effects (page 3, lines 27-29; page 9, lines 28-35). PH modifiers include ascorbic aid (vitamin C), claimed in claims 11 and 24 (page 10, line 26). The compositions of the reference find uses in traumatically lacerated tissues, claim 22 (page 4, lines 6-12).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide composition and method for sealing the wound using composition comprising cyanoacrylate, pore forming agent and active substance as disclosed by WO '374 and select the octyl and butyl cyanoacrylate monomers as they are preferred by WO '760 because the compositions comprising them are useful as tissue adhesive or sealants that find uses in traumatically lacerated tissues, a function desired by applicants, and they form a composition of adequate flexibility and strength that is maintained as natural tissue healing proceeds, and also one having ordinary skill

in the art would have been motivated to add anti-degradation agents such as vitamin C disclosed by WO '760 to the sealing composition of WO '374 motivated by the teaching of WO '760 that these compounds regulate the polymer biodegradation and make it proceeds more slowly than it does at a physiological pH resulting in retarding the rate of release of the degradation products, thereby reducing their toxic effects with reasonable expectation of having safe non toxic wound sealant with sustained sealing effect.

15. Claims 6 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO '374 in view of WO 99/20685 ('685).

The teachings of WO '374 are discussed above.

WO '374 does not teach the molecular weight of the polyethylene glycol as claimed in claims 6 and 18.

WO '685 teaches a formulation that forms a film comprising water soluble pore forming agent such as polyethylene glycol that leaches out through the film in situ and creates a perforations that regulate the release rate of active agents (page 7, lines 10-16). The preferable molecular weight of the polyethylene glycol that is able to create adequate pore size for controlling the release of the active agents is from 540 to 8000, i.e. encompasses the molecular weight claimed by applicants in claims 6 and 18 (page 9, lines 23-28; page 10, lines 1-2).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide composition and method for sealing the wound using composition comprising cyanoacrylate, polyethylene glycol as pore forming agent and

active substance as disclosed by WO '374 and select the molecular weight of the polyethylene glycol between 540 and 8000 as taught by WO '685 because this range of molecular weight is preferred by the WO '685 because of the ability of polyethylene glycol having such molecular weight to create adequate pore size for controlling the release of the active agents, with reasonable expectation of success of the delivered wound sealing composition to deliver active agents at a controlled rate to the wound site with success.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (703) 305-4048. The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Isis Ghali
Examiner
Art Unit 1615

Isis Ghali